

## Gene Section

### Mini Review

# SOX10 (SRY (sex determining region Y)-box 10)

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## Identity

**Other names:** DOM, MGC15649, WS2E, WS4

**HGNC (Hugo):** SOX10

**Location:** 22q13.1

**Local order:** Flanked by POLR2F (DNA-directed RNA polymerase II polypeptide F) and PICK1 (protein interacting with PRKCA 1).

## DNA/RNA

### Note

SOX10 was first identified as a gene mutated in patients suffering from Waardenburg syndrome type 4C (WS4C). SOX10 mutations also cause Waardenburg syndrome type 2E (WS2E) with or without neurologic involvement, Yemenite deaf-blind hypopigmentation syndrome and PCWH syndrome. They usually occur in the heterozygous state and can be either sporadic or familial.

### Description

DNA size: 12.22kb; 5 Exons.

### Transcription

mRNA size: 2882 nucleotides.

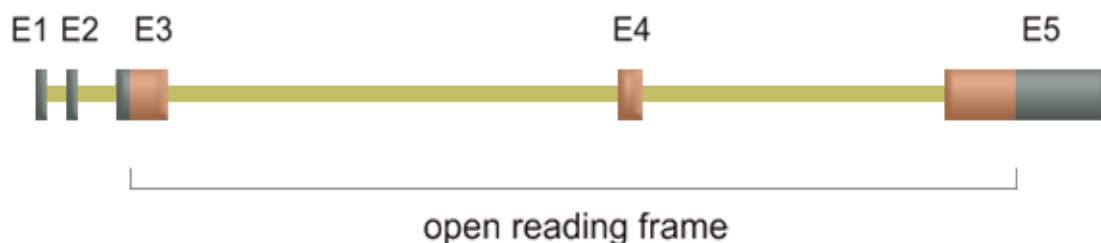
## Protein

### Note

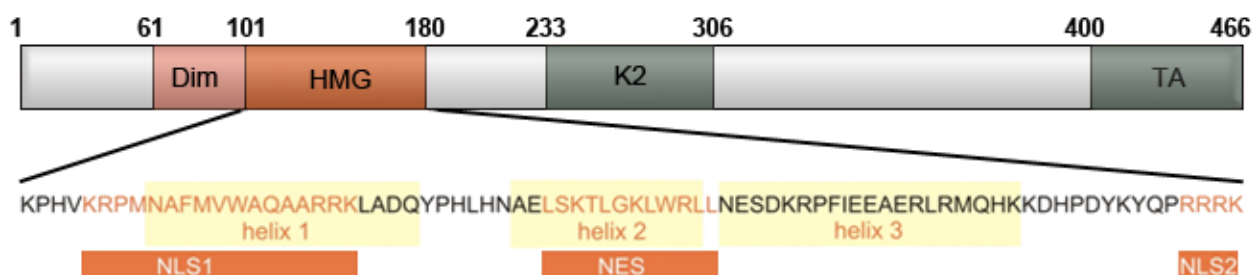
The SOX10 protein belongs to subgroup E of the SOX protein family. All 20 human members of this protein family possess a high-mobility-group (HMG) domain with three alpha-helical regions and close similarity to the one found in the male sex determining factor SRY. SOX10 functions as transcription factor and structural protein in chromatin. SOX9 and SOX8 are its closest relatives among human SOX proteins.

### Description

SOX10 consists of 466 amino acids. The following domains exist (from amino terminal to carboxy terminal): DNA-dependent dimerization domain (amino acids 61-101), DNA-binding HMG-domain (amino acids 101-180), context-dependent transactivation domain K2 (amino acids 233-306) and main transactivation domain TA (amino acids 400-462). SOX10 possesses two nuclear localization signals (NLS) at the beginning and the end of the HMG domain and a nuclear export sequence (NES in the middle).



The SOX10 gene with its 5 exons. The open reading frame (orange) is split between exons 3-5. The 5' untranslated region is generated from exons 1-3 and the 3' untranslated region corresponds to the hind part of exon 5.



Human SOX10 and its domains including the DNA-dependent dimerization domain (Dim), the DNA-binding HMG domain, the context-dependent transactivation domain K2 and the main transactivation domain (TA). Numbers indicate amino acid positions. The bottom shows the exact amino acid sequence of the HMG domain with its three alpha-helices, the 2 nuclear localization signals (NLS1, NLS2) and the nuclear export sequence (NES).

## Expression

SOX10 expression is first detected during embryonic development in the emerging neural crest and continues transiently or permanently in many non-ectomesenchymal derivatives of the neural crest including melanocytes, adrenal medulla and the developing peripheral nervous system. Within the developing central nervous system SOX10 marks cells of the oligodendrocyte lineage. In the adult, SOX10 is predominantly found in oligodendrocytes, peripheral glial cells, melanocytes and adult neural crest stem cell populations.

## Localisation

SOX10 is predominantly found in the nucleus as expected for a transcription factor but possesses the ability to shuttle between cytoplasm and nucleus because of the presence of both NLS and NES in the protein.

## Function

SOX10 has multiple roles during development. In neural crest stem cells, SOX10 is needed for self-renewal, survival and maintenance of pluripotency. SOX10 is furthermore required for specification of melanocytes and peripheral glia from the neural crest. After specification, SOX10 continues to be essential for lineage progression and maintenance of identity in peripheral glia. Terminal differentiation of oligodendrocytes also depends on SOX10. SOX10 exerts these functions through interactions with different sets of transcription factors. SOX10 probably shares further roles with its close relatives SOX9 and SOX8 with which it is co-expressed in several cell types and functions in a partly redundant manner.

## Homology

SOX10 is highly conserved among vertebrates. Human SOX10 shares 98% identity with *Mus musculus* Sox10, 97% identity with Sox10 from *Rattus norvegicus* and *Canis lupus familiaris*, 96% identity with *Bos taurus* Sox10 and 82% identity with *Gallus gallus* Sox10.

## Mutations

### Note

SOX10 mutations have so far primarily been identified as a cause for neurocristopathies including WS4C, WS2E with or without neurologic involvement, PCWH syndrome and Yemenite deaf-bling hypopigmentation syndrome.

### Germinal

**Missense mutations:** S135T, A157V, Q174P.

**Nonsense mutations:** R43X, T83X, T173X, E189X, T207X, Q234X, Q250X, S251X, T313X, S346X, Q364X, Q372X, S376X, Q377X.

**Insertions:** (L160 R161) dup.

**Carboxy terminal extensions:** X467C ext82, X467L ext86, X467T ext86.

**Frameshift mutations:** S17C fsX17, E57S fsX57, A110L fsX2, P169R fsX117, R215P fsX64, R261A fsX25, G266A fsX20, I271S fsX15, H283L fsX11, H306T fsX5, G308A fsX3, V350C fsX52, A354P fsX3, E359D fsX42, Q399V fsX2.

**Splice mutations:** int3 pos.428 +2T>G, int4 pos.698 -2A>C.

### Somatic

**Missense mutations:** R43Q, Q125X, A361V, G413S, G413D, H414Y, A424V.

**Frameshift mutations:** P14P fsX10, S449S fsX66.

## Implicated in

### Melanoma

#### Note

SOX10 is expressed homogenously in primary and metastatic melanoma and was identified as a melanoma tumor antigen. It is often co-expressed with its relative SOX9. Somatic SOX10 mutations occur in early stage melanoma. SOX10 upregulates MITF, MET and Nestin expression in melanoma and responds to Wnt signals. Its nuclear localization is controlled by the Tam tyrosine receptor kinase Tyro3 and its activity is

modulated by the transcription factor SOX5. In sentinel lymph nodes, SOX10 is a reliable marker for metastatic melanoma.

### ***Clear cell sarcoma***

#### **Note**

SOX10 is widely expressed in clear cell sarcoma where it cooperates with EWS-ATF1 fusions in MITF activation.

### ***Malignant nerve sheath tumor (MNST)***

#### **Note**

SOX10 is present in MNST. Expression levels appear lower than the ones in plexiform neurofibromas from which MNST arise or in Schwann cells. SOX10 expression levels are positively correlated with ErbB3 levels and inversely correlated with SOX9 levels.

### ***Schwannoma***

#### **Note**

Homogenous SOX10 expression has been detected throughout this neoplasm.

### ***Ganglioneuroma***

#### **Note**

SOX10 expression has been detected. Levels decrease with increasing grade.

### ***Glioma***

#### **Note**

SOX10 transcripts and protein were found in astrocytoma, oligodendroglioma and glioblastoma. Expression levels and number of expressing cells within the tumor usually diminish with advancing grade and malignant progression. SOX10 levels are particularly high in pilocytic astrocytoma. No correlation with 1p and 19q deletions has been detected. In a mouse model, SOX10 has been found to act synergistically with PDGF during glioma development, although it was not sufficient to induce gliomagenesis on its own.

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